

(19) World Intellectual Property
Organization
International Bureau



542 704

(43) International Publication Date
12 August 2004 (12.08.2004)

PCT

(10) International Publication Number
WO 2004/067021 A1

- (51) International Patent Classification⁷: **A61K 38/00**, C07K 5/00, 14/00
- (21) International Application Number:
PCT/US2003/002155
- (22) International Filing Date: 24 January 2003 (24.01.2003)
- (25) Filing Language: English
- (26) Publication Language: English
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- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— with international search report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: CONFORMATIONALLY CONSTRAINED PARATHYROID HORMONE (PTH) ANALOGS WITH LACTAM BRIDGES

(57) Abstract: The present invention relates to methods of treatment of mammalian conditions characterized by decreases in bone mass with conformationally constrained parathyroid hormone (PTH) analogs and derivatives of those analogs containing PTH polypeptide derivatives containing at least one Glu or Lys substitution at position 6 and/or 10, some with installed lactam bridges between the side chains of Lys and Glu. The invention provides derivatives of PTH (1-34), PTH(1-33), PTH(1-32), PTH(1-31), PTH(1-30), PTH(1-29), PTH(1-28), PTH(1-27), PTH(1-26), PTH(1-25), PTH(1-24), PTH(1-23), PTH(1-22), PTH(1-21), PTH(1-20), PTH(1-19), PTH(1-18), PTH(1-17), PTH(1-16), PTH(1-15), PTH(1-14), PTH(1-13), PTH(1-12), PTH(1-11), PTH(1-10) and PTH(1-9) polypeptide. The invention also provides methods of preparing the PTH analogs. Further, the invention encompasses treating conditions that are characterized by undesired bone loss or by the need for bone growth, e.g. in treating fractures or cartilage disorders and for raising cAMP levels in cells where deemed necessary.

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